UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/639,207	08/14/2000	Parsa Kazemi-Esfarjani	06618-686001	9459

20985 7590 02/28/2002

FISH & RICHARDSON, PC
4350 LA JOLLA VILLAGE DRIVE
SUITE 500
SAN DIEGO, CA 92122

EXAMINER
PAPPU, SITA S

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/28/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/639,207	KAZEMI-ESFARJANI ET AL.	
	Examiner	Art Unit	
	Sita Pappu	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-79* is/are pending in the application.

4a) Of the above claim(s) *47-49 and 51-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-46 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2,4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants election, without traverse, of Group I claims 1-25, 26-46 and 50 in Paper #6 01/16/02 is acknowledged. Claims 47-49, 51-79 are withdrawn from consideration, and are not cancelled, as requested. Currently, claims 1-79 are pending in the instant application. This paper contains an examination of claims 1-46 and 50 on their merits.

Oath/Declaration

Declaration is not legible.

Specification

Text is missing. Page 2, line 2 is missing a closed parenthesis. Page 6, line 30; page 36, line 2; page 73, line 20 are missing the end of the sentence.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-46 and 50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening for genes that modulate polyglutamine toxicity comprising: providing a Drosophila melanogaster expressing a polyglutamine sequence, wherein the sequence produces polyglutamine toxicity in Drosophila melanogaster, and breeding the first Drosophila melanogaster to a second D. melanogaster, wherein the second D. melanogaster has a P transposable element inserted into its germline, thereby producing progeny, and screening the

progeny for increased or decreased polyglutamine toxicity relative to the first D. melanogaster, and identifying one or more genes adjacent to or having an insertion of the P element sequence that confers increased or decreased polyglutamine toxicity in the progeny having increased or decreased polyglutamine toxicity, does not reasonably provide enablement for a method of screening for genes that modulate polyglutamine toxicity in any and all animals, and not any and all invertebrates, and not with any and all Drosophila melanogaster having polyglutamine toxicity as the first parent, other than those D. melanogaster exhibiting polyglutamine toxicity due to the expression of a polyglutamine sequence residing on the expression construct of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In the instant case, claims 1-46, and 50 are drawn to a method of screening for genes that modulate polyglutamine toxicity comprising: providing a first animal expressing a polyglutamine sequence, wherein the sequence produces polyglutamine toxicity in the animal, and breeding the first animal to a second animal, wherein the second animal has a marker sequence inserted into its germline, thereby producing progeny, and screening the progeny for increased or decreased polyglutamine toxicity relative to the first animal, and identifying one or more genes adjacent to or having an insertion of the marker sequence that confers increased or decreased polyglutamine toxicity in the progeny having increased or decreased polyglutamine toxicity.

The claims encompass a method of screening for genes that modulate polyglutamine toxicity comprising the method of claims 1-46 and 50 in any and all animals, and any and all invertebrates, and with any and all Drosophila melanogaster having polyglutamine toxicity due to any reason, as the first parent. The specification only discloses a method of screening for genes that modulate polyglutamine toxicity using Drosphila melanogaster as the first parent, that is expressing a polyglutamine sequence, wherein the sequence produces polyglutamine toxicity in Drosophila melanogaster, and breeding the first Drosophila melanogaster to a second D. melanogaster, wherein the second D. melanogaster has a P transposable element inserted into its germline, thereby producing progeny, and screening the progeny for increased or decreased polyglutamine toxicity relative to the first D. melanogaster, and identifying one or more genes adjacent to or having an insertion of the P element sequence that confers increased or decreased polyglutamine toxicity in the progeny having increased or decreased polyglutamine toxicity. The specification does not disclose a method of screening for genes that modulate polyglutamine toxicity in any and animals and any and all invertebrates using the method of the instant invention.

For example, it is known in the art that the P-transposable elements are specific to Drosophila. Loukeris et al. (1995, Science, vol. 270, pp 2002-2005) state that the P-element mediated germline transformation system does not function in other Drosophila species and that attempts to introduce P element into mosquitoes have yielded only rare germline transformation events that represent random integration of DNA segments including plasmid sequences, instead of transposase-mediated insertions of the

transposable element alone (page 2002, middle column, first paragraph of the article, lines 9-17). Although, Loukeris et al. (1995) demonstrated the introduction of Drosophila hydei transposable element Minos into the Mediterranean fruit fly, Ceratitis capitata, it is unpredictable whether a skilled artisan would be able to achieve success in the germ line transformation of any and all animals, with the P transposable element of Drosophila melanogaster.

In the absence of specific guidance, it is unpredictable how the P element from Drosophila melanogaster would be inserted into the genome of any and all animals and what the resulting phenotype would be, for one of skill in the art to select the parents for breeding in the method of screening for progeny that exhibit increased or decreased polyglutamine toxicity such that a skilled artisan would arrive at the progeny and genes that modulate polyglutamine toxicity in any and all animals, using the method of the present invention. The breadth and scope of claims 1-46 and 50, thus, surpass that enabled by the specification. Even though the skill of an artisan in this subject area is considered to be very high, it would require undue experimentation on the part of an artisan to make and use the claims as specified and use the invention as claimed. The specification and the working examples provide sufficient guidance to practice the invention with only a Drosophila melanogaster expressing a polyglutamine sequence, wherein the sequence produces polyglutamine toxicity in Drosophila melanogaster, and breeding the first Drosophila melanogaster to a second D. melanogaster, wherein the second D. melanogaster has a P transposable element inserted into its germline, thereby producing progeny, and screening the progeny for increased or decreased

polyglutamine toxicity relative to the first D. melanogaster, and identifying one or more genes adjacent to or having an insertion of the P element sequence that confers increased or decreased polyglutamine toxicity in the progeny having increased or decreased polyglutamine toxicity. However, neither the specification nor the working examples provide enough guidance on how to practice the invention with any and all animals and invertebrates as claimed.

With regard to claim 50, step (b), specification does not disclose how to detect polyglutamine toxicity in a single cell of any animal as claimed. Without sufficient guidance on how to detect and assay for the polyglutamine toxicity and the suppression and/or enhancement of the said toxicity in any animal as claimed, it would be unpredictable how to identify and/or detect and assay for the polyglutamine toxicity in any and all animals and it would require undue experimentation on the part of a skilled artisan to make and use the invention of claim 50 as claimed.

Thus, the specification is not enabling for a method of screening for genes that modulate polyglutamine toxicity in any animal and any invertebrate using the method of the claimed invention. Therefore, based on the lack of guidance in the specification as to how to make and use the invention with any animal and/or invertebrate as the parental strain in each generation of breeding for progeny, such that one of skill in the art would be able to identify genes that modulate polyglutamine toxicity, using the claimed method of the instant invention, and the breadth of the claims, it would have required undue experimentation for the skilled artisan at the time of filing to practice the full scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-6, 8, 9, 21, 33, 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite in its recitation of "wherein the first and second animals". It is not clear which second animal the applicants are referring to. Changing the claim language to "wherein the first and the second animals" is suggested.

Claim 5 is indefinite in so far as it depends from claim 4.

Claim 5 is indefinite in its recitation of "genus Drosophila melanogaster". It is not clear whether the term 'genus' is referring to Drosophila or to Drosophila melanogaster. The accepted usage of the term Drosophila melanogaster in taxonomy is such that Drosophila refers to the Genus and melanogaster refers to the species within the genus Drosophila. Correction is required.

Claim 6 is indefinite in its recitation of "wherein the marker sequence comprises a P element", wherein P element can be any type of element. It is suggested to change the claim language such that it reads "wherein the marker sequence comprises a P transposable element".

Claim 8 is indefinite in its recitation of "an expression control element conferring expression of one or more genes". It is not clear how an expression control element can confer expression of the genes. In the accepted usage of English language, it can either

confer expression on the genes or it can control and/or regulate the expression of the genes. Correction is required.

Claim 9 is indefinite in so far as it depends from claim 8.

Claim 9 is indefinite in its recitation of "one or more of the near genes". It is not clear whether the term 'near' is referring to the name of the gene or genes. Changing the claim language such that it reads "one or more of the genes that are adjacent to the expression control element", would make the meaning more clear.

Claims 21 and 33 are indefinite in their recitation of "constitutive, regulatable or tissue specific expression control element". It is not clear how an expression control element can be constitutive and regulatable at the same time. Correction is required.

Claim 50 is indefinite in its recitation of "a length sufficient to produce polyglutamine toxicity". Applicant is advised to specifically point out the length of polyglutamine sequence needed to produce polyglutamine toxicity in the recited Drosophila or to point to a definition for this term in the specification.

Claim 50 is missing an essential step because the egg is never fertilized and you cannot produce an animal from an unfertilized egg.

Claim 50 is missing other steps. The method of claim 50 does not include the step of implanting the embryo into a female for development. The claim is directed to any animal, and for most animals the step of implantation into a female animal is a required step for progeny development.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4-16, 20-35, 41, 42, 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warrick et al. (1998; Cell, vol. 93, pp 939-949) and Tsubota et al. (1985; Molecular and Cellular Biology, vol. 5, no. 10, pp. 2567-2574).

Warrick et al. (1998) expressed human SCA3/MJD protein in Drosophila and recreated the glutamine-repeat disease in Drosophila (see summary, page 939) and demonstrated that cellular mechanisms of human glutamine-repeat disease are conserved in invertebrates using the GAL4-UAS transformation system.

Warrick et al. (1998) do not teach a method of screening for genes modulating polyglutamine toxicity using their system.

Tsubota et al. (1985) demonstrated P element-mediated germline transformation of Drosophila as a way of inducing hybrid dysgenesis and produce mutations in a gene as a way of studying control of gene expression in Drosophila (see summary) and screening for expression modulating mutations at the rudimentary locus in Drosophila (see summary, page 2567).

Tsubota et al. (1985) do not teach their system of screening, for genes that modulate polyglutamine toxicity.

Warrick et al. (1998) produced a Drosophila containing polyglutamine sequence and exhibiting polyglutamine toxicity. Tsubota et al. (1985) revealed a P strain of Drosophila that contains integrated P elements in its genome. Warrick et al. provided the motivation to use his Drosophila in studying polyglutamine toxicity by stating that their fly model will aid in identifying additional factors that modulate neurodegeneration (summary, lines 15-17). At the time of filing, it was well known in the art of Drosophila genetics that P element-mediated hybrid dysgenesis is one of the very common modes of studying Drosophila genetics and control of gene expression, and that it is very useful for identifying genes controlling various phenotypes in Drosophila.

Therefore, it would have been obvious to one of ordinary skill in the art to be motivated to combine the methods of Warrick et al. (1998) and Tsubota et al. (1985) and arrive at a method of screening for genes modulating polyglutamine toxicity in Drosophila. A reasonable expectation of success would have been anticipated because Warrick et al. (1998) had already successfully demonstrated with their fly model that cellular mechanisms modulating glutamine toxicity are conserved in Drosophila.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sita S Pappu whose telephone number is (703) 305-5039. The examiner can normally be reached on Mon-Fri (8:30 AM - 5:00 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (703) 305 1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746 7442 for regular communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Tracey Johnson, whose telephone number is (703) 305-2982.

Anne-Marie Baker

ANNE-MARIE BAKER
PATENT EXAMINER

S. Pappu
February 22, 2002